Microengineered Scaffolds to Guide Cell Assembly

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Abstract

The primary goal of this project is to demonstrate a new approach for guiding cell migration along set paths in a predetermined direction using microengineered scaffolds. Micropatterned biomaterials were used to control the cell size and shape to amplify the natural directional persistence of migrating cells. Using this approach, we can amplify this directional persistence to coerce the migration of cells indefinitely along arbitrary paths in one preset direction without chemoattractants, gradients in substrate adhesiveness, or external fields. The ability to control cell movement on the biomaterials can promote self assembly of multiple cell types for tissues engineering.

Introduction

Tissues engineered *in vitro* can be used to restore and repair human tissues, potentially saving the lives of some patients waiting for organ donation. To engineer tissues *in vitro*, cells are grown on bioactive and degradable scaffolds that provide the physical and chemical cues to guide cell assembly[1]. One major challenge in engineering complex tissues is directional control of cell movement. For example, different cell types assemble in specific patterns to form functional organs, capillaries sprout in the direction of new tissues or wounds, and neural cells migrate in specific directions during formation or regeneration of nervous systems. To date, the primary techniques for inducing cells to migrate into scaffolds rely on chemical cues released from bioactive materials. Coaxing cells to assemble into tissue patterns with dimensions ranging from micron to centimeter length scales remains a challenge. Scaffold designs incorporating *physical* cues to guide the organization and migration of cells are largely unexplored. Part of this is due to the lack of experimental techniques that are capable of providing spatial guidance to direct cell migration.

Here we investigate a completely new approach for controlling the directional migration of cells using micropatterned biodegradable scaffolds. Studies have shown that mammalian cells can respond to physical cues on the surface by spatially redistributing their extracellular matrix[2]. We apply this knowledge in the design of biodegradable scaffolds to demonstrate the controlled migration of cells along a predetermined path and direction.

Materials and methods

Microfabrication has been a useful tool for biology[3-5]. Patterned biomaterials were fabricated using a two step soft lithography and microcontact printing procedure. Silicon patterns with designed shapes were fabricated on silicon wafers using standard photolithographic techniques. From this silicon master pattern, complementary polydimethylsiloxane (PDMS) replicas were formed. Micropatterned chitosan and gelatin films were formed from microcontact printing with poly (OEGMA/MA). Human microvascular endothelial cells or fibroblasts were cultured on the microengineered scaffold and the migration was imaged with Nikon TE 2000 phase contrast microscopes.

Results and Discussion

To understand how cell shape can be used to direct cell migration, we examined the role of cell shape on lamellipodia extension - the first step of cell migration. Human microvascular endothelial cells plated on these biodegradable micropatterned substrates adapt to the shape of the adhesive islands and organize their cytoskeleton and focal adhesion points according to the shape of their confining matrix islands. Our results have demonstrate that lamellipodia preferentially extend from sharp corners that due to the original micropattern designs.

Based on the relationship between cell shape and migration, we have designed specific arrays of micropatterns, to coax cell migration along a predetermined path and direction as shown in Figure 1. Single cells on the tear -shaped adhesive islands extends lamellipodia from the sharp tips and “hop” to neighboring adhesive islands.

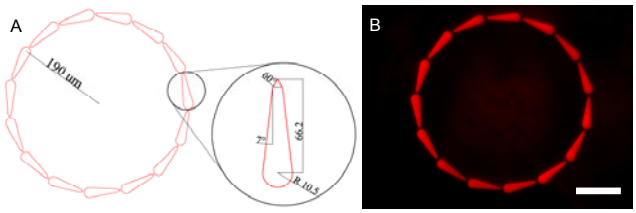

Figure 1. A Schematic of the adhesive islands on microengineered scaffolds B Fluorescence micrograph of the micropatterns stained with labelled protein

References

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